Corporate Medical Policy: Erythropoiesis-Stimulating Agents (ESAs)

Restricted Product(s):

- epoetin alfa (Epogen®) intravenous or subcutaneous injection for administration by a healthcare professional
- epoetin alfa (Procrit®) intravenous or subcutaneous injection for administration by a healthcare professional
- epoetin alfa-epbx (Retacrit®) intravenous or subcutaneous injection for administration by a healthcare professional
- darbepoetin alfa (Aranesp®) intravenous or subcutaneous injection for administration by a healthcare professional
- methoxy polyethylene glycol (PEG) epoetin-beta (Mircera®) for intravenous or subcutaneous injection for administration by a healthcare professional

FDA Approved Use:

- Epoetin alfa (Epogen®)
    - Treatment of anemia due to
        - Chronic Kidney Disease (CKD) in patients on dialysis and not on dialysis
        - Zidovudine in patients with HIV-infection
        - The effects of concomitant myelosuppressive chemotherapy, and upon initiation, there is a minimum of two additional months of planned chemotherapy
    - Reduction of allogeneic RBC transfusions in patients undergoing elective, noncardiac, nonvascular surgery
- Epoetin alfa (Procrit®)
    - Treatment of anemia due to
        - Chronic Kidney Disease (CKD) in patients on dialysis and not on dialysis
        - Zidovudine in patients with HIV-infection
        - The effects of concomitant myelosuppressive chemotherapy, and upon initiation, there is a minimum of two additional months of planned chemotherapy
    - Reduction of allogeneic RBC transfusions in patients undergoing elective, noncardiac, nonvascular surgery
- Epoetin alfa (Retacrit®)
    - Treatment of anemia due to
        - Chronic Kidney Disease (CKD) in patients on dialysis and not on dialysis
        - Zidovudine in patients with HIV-infection
        - The effects of concomitant myelosuppressive chemotherapy, and upon initiation, there is a minimum of two additional months of planned chemotherapy
    - Reduction of allogeneic RBC transfusions in patients undergoing elective, noncardiac, nonvascular surgery

- Darbepoetin alfa (Aranesp®)
    - Treatment of anemia due to:
        - Chronic Kidney Disease (CKD) in patients on dialysis and patients not on dialysis
        - The effects of concomitant myelosuppressive chemotherapy, and upon initiation, there is a minimum of two additional months of planned chemotherapy
- Methoxy polyethylene glycol (PEG) epoetin-beta (Mircera®)
    - Treatment of anemia associated with chronic kidney disease (CKD) in:
        - Adult patients on dialysis and adult patients not on dialysis
        - Pediatric patients 5 to 17 years of age on hemodialysis who are converting from another ESA after their hemoglobin level was stabilized with an ESA

Criteria for Medical Necessity:

The restricted product(s) may be considered medically necessary when the following criteria are met:

Criteria for Approval of Restricted Product(s):

1. The patient's transferrin saturation, serum ferritin, and hemoglobin have been evaluated (in the last 4 weeks); **AND**
2. For patients with a serum ferritin of < 100 mcg/L or a serum transferrin saturation < 20%, supplemental iron therapy has been initiated; **AND**
3. The patient will be using the product to reduce allogeneic transfusions; **AND**
    a. The patient is a candidate for elective, noncardiac, nonvascular surgery; **AND**
    b. The patient's hemoglobin is > 10 g/dL and ≤ 13 g/dL; **OR**
4. The patient will be using for anemia due to myelosuppressive chemotherapy; **AND**
    a. The patient has a non-myeloid malignancy; **AND**
    b. The patient's hemoglobin is < 10 g/dL (in the last 4 weeks); **AND**
    c. The patent is currently on or has received chemotherapy in the last 6 months; **AND**
    d. Chemotherapy is not intended to be curative; **AND**
    e. The requested medication is NOT Mircera; **OR**
5. The patient will be using for anemia associated with chronic kidney disease; **AND**
    a. The patient has been diagnosed with chronic kidney disease; **AND**
    b. The patient is on dialysis with a hemoglobin of < 10 g/dL (in the last 4 weeks); **OR**

   c. The patient is not on dialysis with a hemoglobin of <10 g/dL (in the last 4 weeks) and is steadily decreasing, indicating a high likelihood for RBC transfusion; **OR**
6. The patient will be using for anemia due to myelodysplastic syndrome; **AND**
   a. The patient has been diagnosed with myelodysplastic syndrome; **AND**
   b. The patient's hemoglobin is < 12 g/dL when starting ESA therapy; **OR**
   c. The patient's hemoglobin is ≤12 g/dL while receiving and stable on ESA therapy; **OR**
7. The patient will be using for anemia related to zidovudine treatment; **AND**
   a. The patient has been diagnosed with HIV/AIDS; **AND**
   b. The patient is being treated with zidovudine; **AND**
   c. The patient's hemoglobin is < 12 g/dL when starting ESA therapy; **OR**
   d. The patient's hemoglobin is ≤ 12 g/dL while receiving and stable on ESA therapy; **OR**
8. The prescriber has submitted documentation in support of the use of the prescribed ESA for the intended diagnosis which has been reviewed and approved by the Clinical Review pharmacist; **AND**
   a. The patient's hemoglobin is < 12 g/dL when starting ESA therapy; **OR**
   b. The patient's hemoglobin is ≤ 12 g/dL while receiving and stable on ESA therapy; **AND**
9. If the request is for Epogen or Procrit, the patient has tried and had an inadequate response to Retacrit OR has an intolerance, FDA labeled contraindication, or hypersensitivity to Retacrit **[medical record documentation required]**.
10. The requested quantity does NOT exceed the maximum units allowed for the duration of approval (see table below).

Duration of Approval:

Reduction of allogenic blood transfusion: 180 days
Anemia due to myelosuppressive chemotherapy: 180 days
All other diagnoses: 365 days

NOTE:

Use of Denosumab may be considered medically necessary for clinical indications not listed above when the drug is prescribed for the treatment of **cancer** either:

1. In accordance with FDA label (when clinical benefit has been established, and it is not determined to be investigational as defined in the Blue Cross NC Corporate Medical Policy (CMP), “Investigational (Experimental) Services.” [please refer to CMP “Investigational (Experimental) Services” for a summary of evidence standards from nationally recognized compendia]; **OR**

2. In accordance with specific strong endorsement or support by nationally recognized compendia, when such recommendation is based on strong/high levels of evidence, and/or uniform consensus of clinical appropriateness has been reached.

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
Epoetin alfa (Epogen®)	Treatment of anemia due to: Chronic Kidney Disease (CKD) in patients on dialysis and not on dialysis Zidovudine in patients with HIV-infection The effects of concomitant myelosuppressive chemotherapy, and upon initiation, there is a minimum of two additional months of planned chemotherapy Reduction of allogeneic RBC transfusions in patients undergoing elective, noncardiac, nonvascular surgery	**Patients with CKD:** Initial dose: 50 to 100 Units/kg 3 times weekly (adults) and 50 Units/kg 3 times weekly (pediatric patients). Individualize maintenance dose. Intravenous route recommended for patients on hemodialysis **Patients on Zidovudine due to HIV-infection:** 100 Units/kg 3 times weekly **Patients with Cancer on Chemotherapy:** 40,000 Units weekly or 150 Units/kg 3 times weekly (adults); 600 Units/kg intravenously weekly (pediatric patients ≥ 5 years) **Surgery Patients:** 300 Units/kg per day daily for 15 days or 600 Units/kg weekly	**Q4081(for CKD dialysis only)** **J0885 (for non-dialysis)**	**CKD:** 15600 **Patients on Zidovudine:** 1560 **Cancer patients on chemotherapy:** 1170 **Reduction of allogenic RBC transfusions:** 450

Epoetin alfa (Procrit®)	Treatment of anemia due to: Chronic Kidney Disease (CKD) in patients on dialysis and not on dialysis Zidovudine in patients with HIV-infection The effects of concomitant myelosuppressive chemotherapy, and upon initiation, there is a minimum of two additional months of planned chemotherapy Reduction of allogeneic RBC transfusions in patients undergoing elective, noncardiac, nonvascular surgery	**Patients with CKD:** Initial dose: 50 to 100 Units/kg 3 times weekly (adults) and 50 Units/kg 3 times weekly (pediatric patients). Individualize maintenance dose. Intravenous route recommended for patients on hemodialysis **Patients on Zidovudine due to HIV-infection:** 100 Units/kg 3 times weekly **Patients with Cancer on Chemotherapy:** 40,000 Units weekly or 150 Units/kg 3 times weekly (adults); 600 Units/kg intravenously weekly (pediatric patients ≥ 5 years) **Surgery Patients:** 300 Units/kg per day daily for 15 days or 600 Units/kg weekly	**Q4081(for CKD dialysis only)** **J0885 (for non-dialysis**	**CKD:** 15600 **Patients on Zidovudine:** 1560 **Cancer patients on chemotherapy:** 1170 **Reduction of allogenic RBC transfusions:** 450
Epoetin alfa-epbx (Retacrit®)	Treatment of anemia due to: Chronic Kidney Disease (CKD) in patients not on dialysis Zidovudine in patients with HIV-infection The effects of concomitant myelosuppressive chemotherapy, and upon initiation, there is a minimum of two additional months of planned chemotherapy	**Patients with CKD:** Initial dose: 50 to 100 Units/kg 3 times weekly (adults) and 50 Units/kg 3 times weekly (pediatric patients). Individualize maintenance dose. **Patients on Zidovudine due to HIV-infection:** 100 Units/kg 3 times weekly **Patients with Cancer on Chemotherapy:** 40,000 Units weekly or 150 Units/kg 3 times weekly (adults); 600 Units/kg intravenously weekly (pediatric patients ≥ 5 years)	**Q5106 (for non-dialysis)**	**CKD:** 15600 **Patients on Zidovudine:** 1560 **Cancer patients on chemotherapy:** 1170 **Reduction of allogenic RBC transfusions:** 450

	Reduction of allogeneic RBC transfusions in patients undergoing elective, noncardiac, nonvascular surgery	**Surgery Patients:** 300 Units/kg per day daily for 15 days or 600 Units/kg weekly		
Darbepoetin alfa (Aranesp®)	Treatment of anemia due to: Chronic Kidney Disease (CKD) in patients on dialysis and patients not on dialysis The effects of concomitant myelosuppressive chemotherapy, and upon initiation, there is a minimum of two additional months of planned chemotherapy	**Starting dose for patients with CKD on dialysis**: 0.45 mcg/kg intravenously or subcutaneously weekly, OR 0.75 mcg/kg intravenously or subcutaneously every 2 weeks **Starting dose for patients with CKD not on dialysis**: 0.45 mcg/kg intravenously or subcutaneously at 4 week intervals **Starting dose for pediatric patients with CKD**: 0.45 mcg/kg intravenously or subcutaneously weekly. **Pediatric patients with CKD not on dialysis may also be** initiated at 0.75 mcg/kg every 2 weeks **Starting dose for patients with cancer on chemotherapy:** 2.25 mcg/kg subcutaneously weekly, or -500 mcg subcutaneously every 3 weeks	**J0882 (for CKD dialysis only** **J0881 (for non-dialysis)**	**CKD on dialysis:** 2340 **Adult CKD not on dialysis:** 585 **Pediatric CKD patients:** 2340 **Cancer Patients on chemotherapy:** 5850
Methoxy polyethylene glycol (PEG) epoetin-beta (Mircera®)	Treatment of anemia associated with chronic kidney disease (CKD) in: Adult patients on dialysis and adult patients not on dialysis.	**Initial Treatment**: 0.6 mcg/kg body weight administered once every two weeks Conversion from Another ESA: dosed once monthly or once every two weeks based on	**J0887 (for CKD dialysis only**	**1560**

	Pediatric patients 5 to 17 years of age on hemodialysis who are converting from another ESA after their hemoglobin level was stabilized with an ESA.	total weekly epoetin alfa or darbepoetin alfa dose at time of conversion	**J0888 (for non dialysis)**	

***Maximum units allowed for duration of approval**

References: all information referenced is from FDA package insert unless otherwise noted below.

Policy Implementation/Update Information:

April: Criteria Update: Added Retacrit dosing for CKD patients not on dialysis to FDA dosing table
March 2022: Criteria change: Removal of code Q5105 from dosing table
June 2021: Criteria change: Added requirement of evaluation of patient's transferrin saturation, serum ferritin, and hemoglobin; requirement of supplemental iron for low ferritin or transferrin; removal of Omontys; defined surgical candidate for reduce allogeneic transfusions as elective, noncardiac, nonvascular; added maximum units; medical policy formatting change. **Policy notification given 4/16/2021 for effective date 6/16/2021**.
*Further historical criteria changes and updates available upon request from Medical Policy and/or Corporate Pharmacy

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Discrimination is Against the Law

- Blue Cross and Blue Shield of North Carolina ("Blue Cross NC") complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex.
- Blue Cross NC does not exclude people or treat them differently because of race, color, national origin, age, disability, or sex.

Blue Cross NC:

- Provides free aids and services to people with disabilities to communicate effectively with us, such as:
  - Qualified interpreters
  - Written information in other formats (large print, audio, accessible electronic formats, other formats)
- Provides free language services to people whose primary language is not English, such as:
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  - Information written in other languages

- If you need these services, contact Customer Service **1-888-206-4697**, TTY and TDD, call **1-800-442-7028**.

- If you believe that Blue Cross NC has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, or sex, you can file a grievance with:
  - Blue Cross NC, PO Box 2291, Durham, NC 27702, Attention: Civil Rights Coordinator- Privacy, Ethics & Corporate Policy Office, Telephone **919-765-1663**, Fax **919-287-5613**, TTY **1-888-291-1783** civilrightscoordinator@bcbsnc.com

- You can file a grievance in person or by mail, fax, or email. If you need help filing a grievance, Civil Rights Coordinator - Privacy, Ethics & Corporate Policy Office is available to help you.

- You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at *https://ocrportal.hhs.gov/ocr/portal/lobby.jsf,* or by mail or phone at: U.S. Department of Health and Human Services 200 Independence Avenue, SW Room 509F, HHH Building Washington, D.C. 20201 **1-800-368-1019, 800-537-7697** (TDD). Complaint forms are available at *http://www.hhs.gov/ocr/office/file/index.html*.

- This Notice and/or attachments may have important information about your application or coverage through Blue Cross NC. Look for key dates. You may need to take action by certain deadlines to keep your health coverage or help with costs. You have the right to get this information and help in your language at no cost. Call Customer Service **1-888-206-4697**.

ATTENTION: If you speak another language, language assistance services, free of charge, are available to you. Call 1-888-206-4697 (TTY: 1-800-442-7028).

ATENCIÓN: Si habla español, tiene a su disposición servicios gratuitos de asistencia lingüística. Llame al 1-888-206-4697 (TTY: 1-800-442-7028).

注意：如果您講廣東話或普通話， 您可以免費獲得語言援助服務。請致電 1-888-206-4697
(TTY：1-800-442-7028）。

CHÚ Ý: Nếu bạn nói Tiếng Việt, có các dịch vụ hỗ trợ ngôn ngữ miễn phí dành cho bạn. Gọi số
1-888-206-4697 (TTY: 1-800-442-7028).

주의: 한국어를 사용하시는 경우, 언어 지원 서비스를 무료로 이용하실 수 있습니다.
1-888-206-4697 (TTY: 1- 800-442-7028)번으로 전화해 주십시오.

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ملحوظة: إذا كنت تتحدث اللغة العربية، فإن خدمات المساعدة اللغوية تتوافر لك بالمجان. اتصل برقم
1-888-206-4697. المبرقة الكاتبة: 1-800-442-7028.

LUS CEEV: Yog tias koj hais lus Hmoob, cov kev pab txog lus, muaj kev pab dawb rau koj. Hu rau
1-888-206-4697 (TTY: 1-800-442-7028).

ВНИМАНИЕ: Если вы говорите на русском языке, то вам доступны бесплатные услуги перевода. Звоните 1-888-206-4697 (телетайп: 1-800-442-7028).

PAUNAWA: Kung nagsasalita ka ng Tagalog, maaari kang gumamit ng mga serbisyo ng tulong sa wika nang walang bayad. Tumawag sa 1-888-206-4697 (TTY: 1-800-442-7028).

સુચના: જો તમે ગુજરાતી બોલતા હો, તો નિ:સુલ્કુ ભાષા સહાય સેવાઓ તમારા માટે ઉપલબ્ધ છે. ફોન કરો
1-888-206-4697 (TTY: 1-800-442-7028).

ចំណាំ៖ ប្រសិនបើលោកអ្នកនិយាយជាភាសាខ្មែរ សេវាកម្មជំនួយផ្នែកភាសាមានផ្តល់ជូនសម្រាប់លោកអ្នកដោយមិនគិតថ្លៃ។ សូមទំនាក់ទំនងតាមរយៈលេខ៖ 1-888-206-4697 (TTY: 1-800-442-7028)។

ACHTUNG: Wenn Sie Deutsch sprechen, stehen Ihnen kostenlos sprachliche Hilfsdienstleistungen zur Verfügung. Rufnummer: 1-888-206-4697 (TTY: 1-800-442-7028).

ध्यान दें: यदि आप हिन्दी बोलते हैं तो आपके लिए मुफ्त में भाषा सहायता सेवाएं उपलब्ध हैं। 1-888-206-4697 (TTY: 1-800-442-7028) पर कॉल करें।

ໂປດຊາບ: ຖ້າວ່າ ທ່ານເວົ້າພາສາ ລາວ, ການບໍລິການຊ່ວຍເຫຼືອດ້ານພາສາ, ໂດຍບໍ່ເສັງຄ່າ, ແມ່ນມີພ້ອມໃຫ້ທ່ານ. ໂທຣ 1-888-206-4697 (TTY: 1-800-442-7028).

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